CASE REPORTS

Chronic Relapsing Q Fever: Treatment with Streptomycin Aureomycin, and Chloramphenicol

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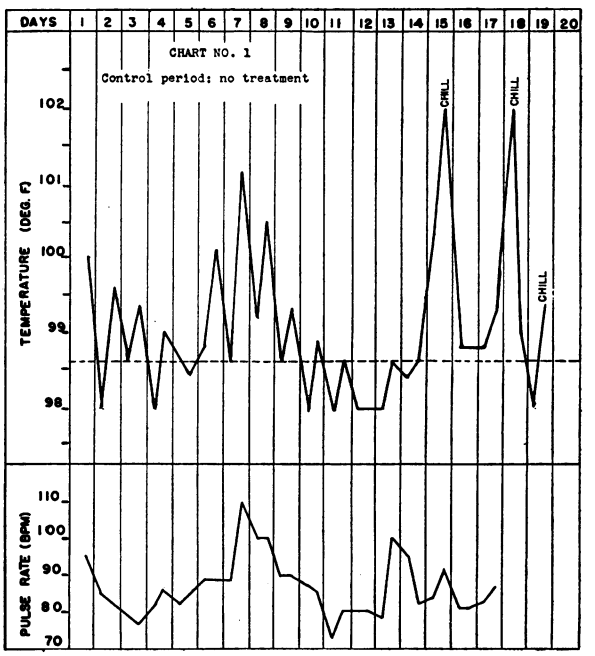
IN a review of the literature, no detailed report of chronic illness attributed to Q fever was found. There follows a description of such a case, which was studied minutely and at great length, although the record is necessarily shortened for publication. Since this case was studied, two additional less severe cases have been observed. Follow-up questionnaires of many patients seen in this area have led to the belief that prolonged asthenic states without actual chronic disease quite commonly follow attacks of acute Q fever.

CASE REPORT

A white male, 38 years of age, was admitted to the Los Angeles County General Hospital Oct. 13, 1948, with a history of recurrent episodes of "shaking chills with fever" for four days which had occurred some seven months previously. At that time, a physician had diagnosed a "flu" syndrome and prescribed a sulfa drug. After about five days, the patient had improved and was well for almost six months until Sept. 10, 1948, when the shaking chills began to recur daily. Fever recurred for more than a week, abated temporarily, then returned; it was associated with pain in the right calf and severe frontal headaches. At that time, an x-ray of the chest was normal. Agglutination tests for brucellosis were negative. The past medical history was irrelevant. The patient had gradually lost approximately 20 pounds in weight since Oct. 1947 for no apparent reason.

At physical examination upon admission, the patient was noted to be well developed and well nourished. The temperature was 100° F., the pulse rate 84 b.p.m., and the blood pressure 120 mm. of mercury systolic and 86 mm. diastolic. Small inguinal nodes were palpable, but there was no other evidence of lymph node involvement. The only other physical findings of note were a tender palpable liver, three finger-breadths below the right costal margin, and a barely palpable spleen.

The patient continued to have shaking chills each morning with fever to 100° F. The spleen gradually diminished in size. Only symptomatic treatment was given. On Nov. 12, 1948, the patient left the hospital with diagnosis not established, and without consent. Blood specimens had been sent to the National Institute of Health at Bethesda for special studies concerning Q fever, but no report had been received at the time the patient left the hospital. The patient returned to his home and soon afterward was visited by the local public health authorities because of two doubtful Kahn test reactions reported by the hospital to the local health department. During the course of the field investigation of the blood studies, reports were received from Bethesda that the complement-fixation reactions for Q fever were positive in a dilution of 1:64. Results of all other bacteriologic and serologic studies were negative.



The patient was readmitted to the Communicable Disease Unit, Jan. 3, 1949, for treatment of Q fever. Since Nov. 12, 1948, he had had nightly sweats with fever of 102° to 103° F., but only two shaking chills. Chief complaints were fever, severe bitemporal headache, and generalized weakness. For a week preceding readmission there had been sharp sticking pains in the left upper quadrant of the abdomen upon deep breathing. The spleen was palpable three finger-breadths below the costal margin. On Jan. 4, 1949, an initial dose of 50 mg. of aureomycin per kilogram of body weight was given orally, followed by a total dose of 500 mg. every four hours. On Jan. 12, the aureomycin dosage was changed to 750 mg. every five hours. Approximately 72 hours after antibiotic therapy was started, the fever subsided and the temperature remained normal until the patient was discharged on Jan. 19, 1949. Prior to discharge, results of Kahn and Wassermann tests of the blood were again reported as doubtful. The albumin-globulin ratio was 3.8:5.3 gm. per 100 cc.

Q-fever complement-fixation titre was reported positive in dilution of 1:134 by the Los Angeles City Health Department and also by the California State Department of Public Health.

At the time of discharge the patient was clinically improved but there was evidence of residual hepatitis. After

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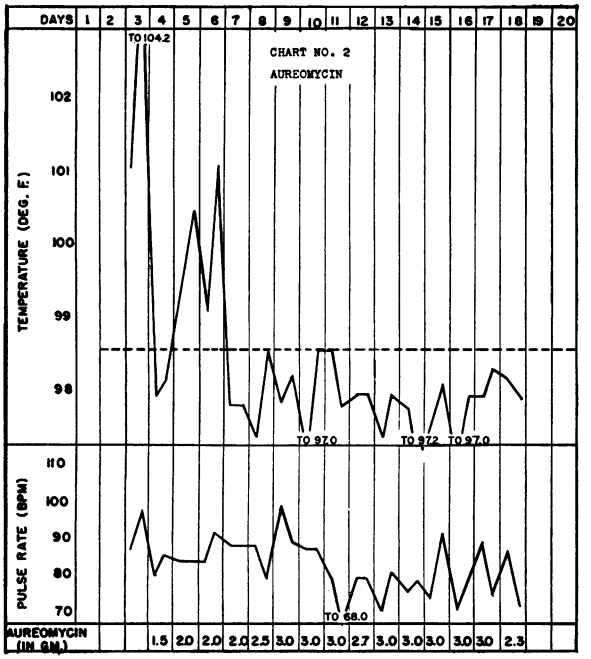
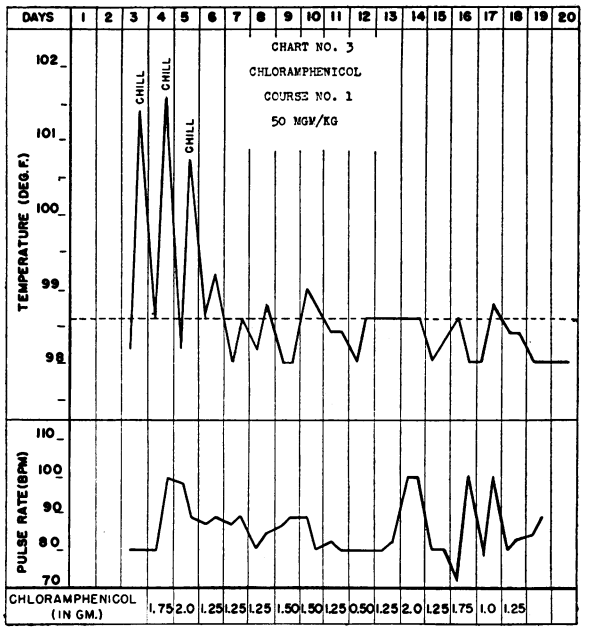
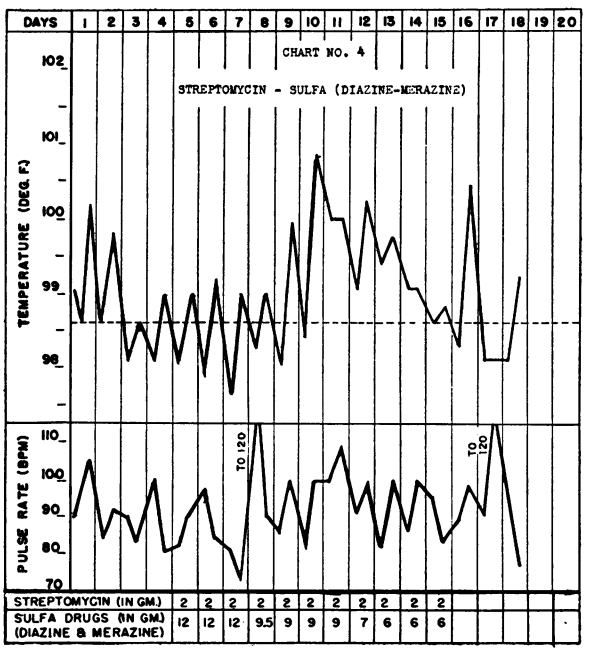






an interval of about two weeks, malaise and occasional backaches developed. At least every other night the temperature reached 101° F., accompanied by severe bitemporal headache. Feb. 9, 1949, the patient had a chill, the first shaking since returning home. He immediately reentered the hospital.

The spleen and liver were palpable approximately three finger-breadths below the costal margins. Because the relapsing course strongly suggested brucellosis, despite completely negative results of laboratory studies, it was decided this time to institute therapy with streptomycin and sulfadiazine. The patient received 1 gm. of streptomycin intramuscularly twice daily, and equal parts of sulfadiazine-sulfamerazine orally (initial dose 4 gm. followed by 1 gm. every four hours) for 11 days. The patient became afebrile in 48 hours, remained so two days, and then the temperature began to rise. Care was taken to maintain adequate concentration of the sulfa drugs in the blood. However, by the tenth day of treatment, fever rose to 101° F. and this treatment was discontinued.

At this time, chloramphenicol* became available for trial, and an initial dose of 50 mg. per kilogram of body weight was divided into three parts which were given in hourly doses. Following these doses, a daily total dosage of 50 mg. per kilogram was given, divided into equal portions on a two-hour schedule around the clock. After the patient became afebrile for 24 hours, the total 24-hour dosage remained on the basis of 50 mg. per kilogram, but was then given every four hours around the clock for an additional 14 days following the first afebrile day. Within 12 hours after the initial dose of chloramphenicol the patient volunteered that he felt very good, but 72 hours elapsed before he became afebrile. Fever did not recur. The patient remained asymptomatic from March 18 through April 1 when he was discharged to his home.

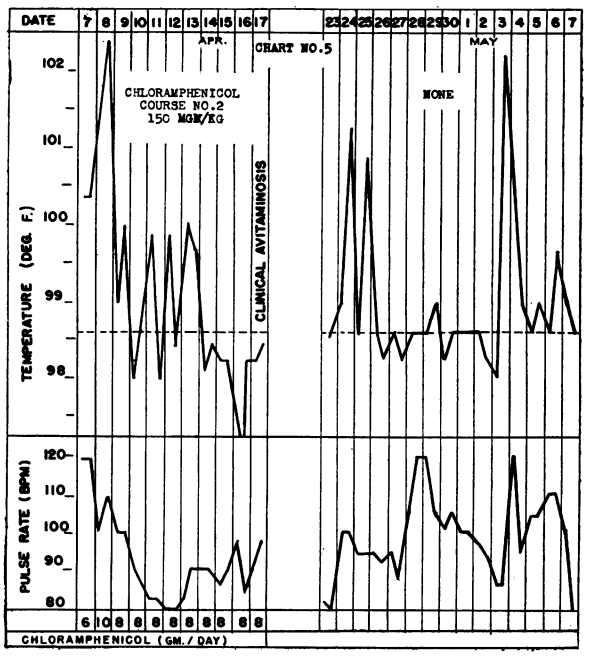
Again, the laboratory reported the results of repeated blood cell counts and urinalyses to be within normal limits. Repeated malaria studies, x-ray films of the chest, blood chemistry determinations, and numerous agglutination tests were non-contributory. The results of Kahn tests, however, were reported as doubtful on two occasions. Three hematocrit determinations showed packed red cells at 40, 37, and 38 per cent of the whole blood. Successive determinations showed albumin-globulin ratios of 3.7:4.3 and 4.1:5.5 gm. per 100 cc., respectively; the icteric index on three occasions never exceeded 10 units; thymol turbidity was 13 units, and the cephalin-cholesterol flocculation was 2 plus in 24 hours. Complement-fixation titres for Q fever were positive in dilutions of 1:520 (March 1), 1:1,032 (March 15), and 1:4,096 (March 31). The determinations were performed by the Los Angeles City Health Department with confirmatory specimens sent to the United States Public Health Service at Bethesda, Md.

During a week at home, the patient daily had fever to 103° F. with profuse nocturnal sweats and shaking chills. He reentered the hospital April 7 for the fourth time with

*The drug was made available by E. C. Von derHeide, M.D., of the Clinical Research Division of Parke, Davis & Co., of Detroit, Michigan.

temperature 100.4° F., pulse rate 120, and respirations 30 per minute. Splenomegaly, hepatomegaly, and a moderate degree of tinea cruris were present. The exanthem in the crural area had been present several weeks before and was now exudative. It was not given unusual consideration.

In view of the previous response, it was decided to use chloramphenicol again, this time in massive dosage on the supposition that previous amounts might have been inadequate and merely suppressive. The staff was not satisfied that the final diagnosis was completely established in this case, and the patient was completely restudied from a laboratory standpoint to ascertain if other entities were present in addition to the indisputable Q fever.



On April 7, an initial dose of 150 mg. of chloramphenicol per kilogram of body weight was divided into three parts and given with one-hour intervals. This was followed by 1 gm. every three hours for the ensuing 14 days. In 72 hours, the patient was subjectively well and completely afebrile. He noted light-headedness, not severe, and a very bitter taste in his mouth. The crural eruption was progressing unfavorably and was annoying. On April 11, prothrombin time (ascertained preparatory to peritoneoscopic visualization) was 49 per cent of normal (normal, 12 seconds). Vitamin K was administered intramuscularly in doses of 10 mg. three times daily. On April 17 there was a generalized, weeping, maculopapular, erythematous eruption, especially pronounced over the forehead, face and thorax; the tongue was beefy red; perleche was present; there was increased conjunctival vascularity and a necklace of erythema of the pellagrinous type. Severe multiple vitamin deficiency was obvious. Dermatologic consultation confirmed this diagnosis on April 20, and the patient was given heavy parenteral dosage of multiple-vitamin preparations. Local applications used until this time had been ineffectual and were stopped. Chloramphenicol was discontinued April 18, following the diagnosis of avitaminosis. After Vitamin K therapy for eight days, prothrombin time was 65 per cent of normal (normal, 14 seconds). Result of a simultaneous cephalin flocculation test was 1 plus in 24 and in 48 hours. The albumin-globulin ratio was reported as 4.1:4.8 gm. per 100 cc. The dermatitis responded rapidly to vitamin therapy parenterally. On April 28, 1949, peritoneoscopic examination was carried out and a biopsy specimen taken from the liver. The postoperative diagnosis based on a macroscopic visualization was hepatitis and subacute splenomegaly. Observations in microscopic examination of tissue sections were reported consistent with "mild cirrhosis, Laennec's type." Because there was still a question of differential diagnosis, especially regarding multiple myeloma or reticuloendotheliosis, serum protein studies by electrophoretic analysis were obtained, with the following report:

	Value (in %)	Normal (in %)
Albumin	30	55–60
Alpha globulin	15	15
Beta globulin	14	14
Gamma globulin	41	12

There was no pattern report which would strongly indicate any specific entity known. Extensive laboratory and roentgenologic data were again non-contributory with the exception of complement-fixation titres positive for Q fever. Complement-fixation titres had progressed to 1:4,096 (May 19), and to 1:16,384 (June 2, 1949).

After seven days of intensive chloramphenicol treatment, the patient was afebrile and felt well, although he had fever of 101° F. on the tenth and eleventh days after the drug was discontinued. Because the dermatitis remained, there was reluctance to resume therapy with any antibiotic which might suppress bacterial action in the intestines. The patient became apprehensive with the return of febrile episodes. Therefore, one of the members of the staff who was investigating the effects of ultraviolet hemo-irradiation by the Knott technique requested permission to treat him by this method. Accordingly, on May 15, 17, and 20, approximately 200 cc. of the patient's own blood was withdrawn, irradiated by the Knott technique and replaced. There was notable euphoria after each treatment. The patient had one sharp episode of fever to 102.4° F. on May 20, but thereafter remained afebrile. The effect of the hemo-irradiation remains a matter of conjecture. The patient was discharged from the hospital May 27, 1949, for follow-up care in the out-patient department. The final discharge diagnoses were:

1. Chronic relapsing Q fever.
2. Hepatitis (cirrhosis of the liver, mild, Laennec's type?)

At about the time the patient was discharged, a belated report was received of agglutination studies done for brucellosis by special technique which included not only removal of the blocking antibodies, but agglutination separately against B. abortus, B. melitensis, and B. suis. The results reported were: For B. abortus, positive in dilutions 1:20 through 1:160, weakly positive in 1:320, negative in 1:640; for B. melitensis, negative in all dilutions; for B. suis, negative in all dilutions.

DISCUSSION

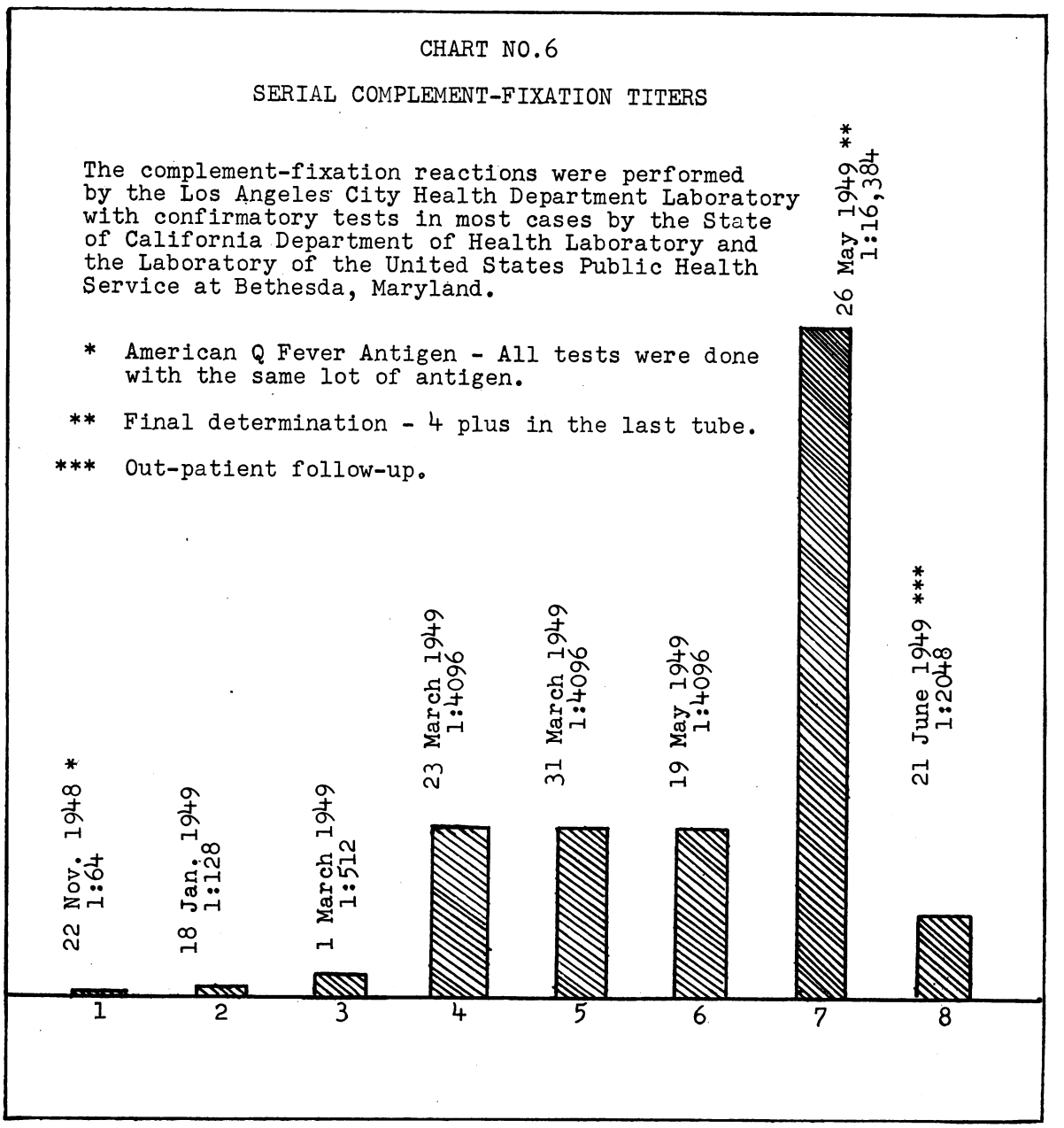
The diagnosis of Q fever was not established during the first hospitalization of the patient, but it was suspected and the resultant positive complement-fixation report from the U.S.P.H.S. established it and indicated rehospitalization for further study and treatment. The second admission was for treatment only, and there was then no suspicion that the case was unusual in any way. By the third admission, Feb. 10, 1949, through April 1, 1949, the bizarre clinical course threw doubt upon the diagnosis, and the patient was subjected to the full scope of diagnostic and therapeutic procedures available. In spite of all efforts to uncover other causes for the illness, the only consistent finding remained a complement-fixation reaction positive for Q fever with a steadily rising titre to 1:16,384 (four plus in the final tube). This titre might have been even higher had the relatively more sensitive Italian antigen been used. While it is known that the complement fixation titre rises in most if not all cases of Q fever during convalescence, the clinical course

of this patient was not that of convalescence, but rather of repeated febrile relapses with each clinical relapse characterized by signs and symptoms usually associated with an initial attack.

Since the diagnosis of Q fever is unequivocally one of laboratory procedures alone, it was necessary to exclude other entities by extensive and repeated determinations. It was also necessary to contrast the clinical course of this illness with those of other entities in order to eliminate conditions for which there are no pathognomonic laboratory findings. If these criteria could be satisfied, the unique diagnosis of chronic relapsing Q fever could be substantiated.

The laboratory findings in clinical Q fever ordinarily revolve about two findings, viz.: pneumonitis and positive complement-fixation titres. In this case, there was at no time clinical or roentgenologic evidence of pneumonitis although x-ray films of the chest were taken six different times. The progress of the complement fixation titres is shown in Figure 6. Erythrocyte and leukocyte counts are usually within normal limits in the presence of Q fever, and they were in this case. Sedimentation rates, electrocardiograms, and cultures of the blood, stools, and urine were not of diagnostic significance. Spicknall[7] reported Coxiella organisms recovered in five of 45 attempts in other cases. In this case, attempts to recover the organism were not made until the fourth admission, and at that time inoculation into animals was unsuccessful. There are no reports of a positive reaction to a Kahn test in Q fever, but it is known that false positives or doubtful reactions may be associated with hepatitis, which was present in this case.

It is of interest to note the low positive agglutination titres obtained during the fourth hospital admission for Brucella abortus. This is in keeping with recent observations by Meyer and Eddie.[5]



The experience with antibiotic therapy was indeed unusual in that the patient appeared clinically to make a good response each time, only to relapse after therapy was stopped. Invariably, under each method of administration the patient became afebrile after 48 to 72 hours of treatment. Subjectively, improvement began even more quickly. In fact, there was virtually euphoria after chloramphenicol was started each time. When the second course of chloramphenicol was instituted with massive dosage, the patient complained of an extremely bitter taste, which can be explained by the fact that this antibiotic is excreted in the saliva within one and a half hours after ingestion.

The development of the classical skin manifestations of avitaminosis, plus the depression of the prothrombin time was not anticipated and, in fact, not recognized early. These occurrences are of much significance. It is apparent that when agents are used which tend to sterilize the bacterial flora of the gastrointestinal tract over prolonged periods, it may be necessary to supplement the treatment with vitamin therapy. In this case, rapid clinical improvement of all general and superficial avitaminotic manifestations occurred when such specific therapy was given.

After the third admission, on Feb. 10, 1949, intensive search was made to determine if more than one disease entity was present. It was known that the patient had hepatitis, but whether this represented a complication of Q fever or was an independent entity, was not known. The patient had never received plasma or blood prior to the present illness. There was never any visible icterus, but the liver and spleen were larger than normal and increased perceptibly in size with each severe febrile relapse. The differential diagnosis and the considerations therein are presented in Table 2.

In all probability, the clinical entity of Q fever has not yet been described in all of its possible variations. The criteria for diagnosis cited by pioneer clinical investigators in this country up to the present are:[1]

1. A four-fold or greater rise in the titre in successive blood specimens during convalescence is considered absolutely diagnostic of Q fever.

2. A single titre of 1:32 or greater during convalescence from an acute febrile illness of a nature clinically compatible with Q fever is considered strongly presumptive of the disease.

In the case here reported, both criteria were met.

The original description of the Australian cases was characterized strikingly by the absence of pneumonitis.[2] It has been present rather consistently in American cases—in 13 of 45 cases of one series,[7] and in 50 of 80 cases in a second series.[1] Absence of pneumonitis, therefore, is not unusual. Its presence, however, is most helpful in suggesting the diagnosis during the initial phases of an illness.

The average incubation period reported is 16 to 18 days, with a range of 13 to 32 days. Although the patient in the case here reported dated the onset of illness to March 1948, it appears more likely that the actual infection occurred

TABLE 1.

Signs and Symptoms Reported in Q Fever from Literature

Symptoms:	(Series of 45 cases[7])	(Series of 80 Cases[1])	Signs and Symptoms in Patient
1. Headache	34	not tabulated	1. Present. With each febrile relapse.
2. Generalized aching	20	10	2. "Flu-like" aching with each relapse.
Arthralgia	0	5	
3. Cough	15	50	3. Absent.
4. Chest pain or discomfort	12	29	4. Absent.
5. Nausea or vomiting	10	26	5. Nausea with each relapse; vomited once.
6. Anorexia	not tabulated	42	6. Present.
7. Burning of eyes	6	3	7. Absent.
8. Bloody sputum	5	not tabulated	8. Absent.
9. Abdominal pain	3	4	9. Epigastric and left upper quadrant pain present.
10. Diarrhea	2	4	10. Absent.
11. Constipation	2	not tabulated	11. Present.
12. Epistaxis	2	not tabulated	12. Absent.
13. Sensitivity of skin	1	4	13. Erythema of forehead and neck with febrile relapses. Tinea cruris.
14. Other	0	0	14. Pain in right calf, second admission.
Signs:			
1. Chills or chilly sensations. Sweats	32	67	1. Bed-shaking chills with febrile episodes.
2. Rales	11	47	2. Absent.
3. Fever without chills or sweats	10	(Fevers 80)	3. Fever with chills and sweats.
4. Abnormal breath sounds in chest	5	21	4. Absent.
5. Conjunctivitis	5	6	5. Absent.
6. Dullness on percussion	4	21	6. Absent.
7. Incr. vocal fremitus	4	not tabulated	7. Absent.
8. Dyspnea	3	not tabulated	8. Absent.
9. Cyanosis	2	not tabulated	9. Absent.
10. Delirium	2	13	10. Absent.
11. Rash	1	4	11. Erythema of face and forehead with fever.
12. Incontinence	1	not tabulated	12. Absent.
13. Palpable liver	not tabulated	3	13. Present.
14. Palpable spleen	not tabulated	2	14. Spleen definitely enlarged.
15. Lymphadenopathy	not tabulated	13	15. Absent.
16. Meningeal irritation	not tabulated	20	16. Absent.

approximately Sept. 10, 1948. At that time, the acute phase began, recurring periodically throughout four periods of hospitalization. The complement-fixation titres increased progressively. The initial positive complement-fixation titre was obtained shortly after the first hospital admission. The usual duration of illness or infection before the appearance of a positive titre is 10 to 14 days.[3]

Six cases in which the patients had relapse following apparent recovery from Q fever have been reported.[2, 4] Heubner and co-workers[3] mentioned a case in which there was complete repetition of the clinical course after a five-day course of treatment with streptomycin. Derrick and Burnet[2] reported one case in which there was a daily rise in temperature for nine weeks after onset of Q fever. The course of illness in that case was approximately nine months.

Sequelae of phlebothrombosis, pains in the legs, edema in the ankles, persisting hiccups, and peripheral claudication have been reported in the literature and have been observed by the authors. The presence of hepatitis as a complication or sequel has not been reported previously.

According to Huebner, significantly high complement-fixation titres have been obtained as long as six years after recovery. In the case here reported, the titre continued to rise progressively with each relapse. With the exceptions of Rocky Mountain spotted fever and brucellosis,[5] no human illnesses have been found to produce serum components capable of giving a positive reaction in the Q fever complement-fixation test.

In the treatment of Q fever, sulfonamides and penicillin have been used singly and in combination, with no perceptible effect. Streptomycin has been reported of value in experimentally induced infections and in isolated clinical instances.[6] Aureomycin is of benefit in human infections.[4] Para-aminobenzoic acid in adequate doses was of no benefit in three reported cases.[1] To the present, there are no reports available concerning the use of chloramphenicol in Q fever. At the time it became available, there was no information concerning optimal dosage and the procedure employed was of a pioneering nature, guided only by clinical judgment and by the information from the manufacturer, who suggested that the dosage originally employed in the pilot studies on scrub typhus be used.

In spite of the fact that the patient remained febrile, a noteworthy feature was the pronounced change in attitude and the feeling of well-being within 24 hours after this antibiotic was given. This euphoric state, however, also occurred when aureomycin was given. Following the relapse after the initial treatment with chloramphenicol, it was decided to use it in massive dosage to rule out inadequate therapy. The second time, the patient noted light-headedness at once, but it was not troublesome enough to warrant discontinuing the therapy. He complained increasingly of a bitter taste which precluded enjoyment of food or drink.

It was midway during this intended 14-day course of treatment that the dermatologic aspects of severe avitaminosis became evident, and for that reason all therapy was stopped. In retrospect, it must be pointed out that following the second hospital admission on Jan. 3, 1949, the patient intermittently received many successive therapeutic agents which are known to sterilize the bacterial content of the gastrointestinal tract. By April 17, 1949, after more than three months of such therapy, avitaminosis was clinically apparent, although the patient was eating an average amount of the usual hospital diet. Unfortunately, the only laboratory determinations—assays, in a sense—which were made to corroborate avitaminosis were the prothrombin-time determinations. That there was associated hepatitis either complicating the Q fever or concomitant with it is unequivocal. It is felt, nevertheless, that the prothrombin time depression was affected by the additional factor of avitaminosis secondary to gastrointestinal bacterial sterilization.

It would appear from this experience that at least two important facts concerning chloramphenicol were brought into clinical focus: The antibiotic is low in toxicity for humans and can be given in relatively large doses comparatively safely; it is wise when chloramphenicol or other similar agents are being administered to use supplements of multiple vitamins especially if therapy is prolonged.

There are at present insufficient autopsy data regarding Q fever to ascertain the anatomical site of Coxiella localization. Despite apparent response to therapy in this case, it is equally apparent that auto-immune mechanisms very probably are required for the eventual suppression. The steady progressive rise in complement-fixation titres is supportive of such a conclusion. Unquestionably, judging by the fever charts, antibiotics can be suppressive and, in many cases, even curative. The latter alternative has been the sole idea

TABLE 2.—*Chronic Relapsing Q Fever*

Conditions Considered in the Differential Diagnosis	Observations and Procedures Used to Include or Exclude This Diagnosis During Four Hospital Admissions:
1. Influenza	1. Length of febrile illness. Serology not attempted.
2. Sinusitis	2. Two series of sinus x-rays. ENT consultations.
3. Malaria	3. Fifteen series of blood smears in all phases of fever. Epinephrine test.
4. Rheumatic fever	4. Two electrocardiograms; 3 sedimentation rates. Clinical picture.
5. Typhus fever	5. Agglutination for OX-19 four times.
6. Brucellosis	6. Blood cultures under special condition, 8; agglutination studies, including those with removal of blocking antibodies, 8.
7. Typhoid fever	7. Blood cultures, 8; stool cultures, 4; urine cultures, 2; agglutination, 6.
8. Psittacosis	8. Complement-fixation, 1. Clinical course.
9. Tuberculosis	9. Skin test positive; chest x-rays, 6.
10. Coccidiomycosis	10. Skin tests, 2—both positive; complement-fixations, 3—all negative.
11. Histoplasmosis	11. Skin tests, 2—both negative.
12. Multiple myeloma	12. Urinalysis, 32; bone marrow studies, 2; body x-rays, 1 complete series. Electrophoretic analysis of serum proteins.
13. Reticuloendotheliosis	13. Bone marrow aspirations, 2; x-rays of bones.
14. Hodgkin's—giant follicular lymphoblastoma, etc.	14. Bone marrow studies, 2; chest x-rays, 6; lack of adenopathy.
15. Lupus erythematosus-periarteritis	15. Urinalyses, 32; complete blood counts, 23.
16. Infectious mononucleosis	16. Heterophil agglutination titres with sheep RBC, 4; blood smears, 12.

up to the present; the former is a relatively newly discovered fact in its relation to the entity of Q fever. Again, a parallel may be made to the history of infectious mononucleosis which only in recent years has become appreciated as a malady of long duration following the subsidence of acute manifestations. Certainly no specific claims of superiority for treatment can be made in this case for streptomycin, aureomycin, or chloramphenicol, since each appeared to be suppressive at least temporarily. It is highly probable that the results of therapy predicated more from the duration of treatment plus continually and increasingly effective auto-immunity than from any specific therapeutic agent utilized.

FOLLOW-UP NOTES

The patient was observed as an out-patient in December 1949, seven months after final discharge from the hospital. He stated that except for pains in the calves of the legs, and ease of fatigue, he had been well since leaving the hospital. The latest blood complement-fixation titre for Q fever (Jan. 18, 1950) was found to be positive in dilutions of 1:2,048 (four plus in final tube).

The patient was seen in July 1950, and stated that he felt well. He stated that his hearing was not as good as it had been before his illness (streptomycin?) and that he still tired easily and had aching in the calves of the legs.

SUMMARY

A case of chronic relapsing Q fever of approximately nine months' duration is reported in detail. Each clinical relapse was characterized by the signs, symptoms, and laboratory data commonly reported in cases of Q fever in humans; each relapse was clinically similar to the preceding phase. Therapy included the use of streptomycin, sulfonamides, aureomycin, and chloramphenicol. Pertinent findings which occurred during therapy are described and discussed especially with relation to prolonged duration of any antibiotic therapy which may have as a side-effect a tendency toward bacterial suppression in the gastrointestinal tract. Reference is made to the fact that the organisms of Q fever produce not only acute clinical entities but also are capable of persistent localization within the body in a manner reminiscent of malarial parasites, and that, in all probability, autoimmune mechanisms are of at least equal importance to antibiotic or other therapy in the eventual cure.

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Progressive Muscular Dystrophy Associated with Retinitis Pigmentosa

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PROGRESSIVE muscular dystrophy and retinitis pigmentosa have been separately found associated with disorders of the endocrine system. The precise relationship between progressive muscular dystrophy and endocrine disturbance is not known. Attention has been called[5] to the occasional association of myopathic dystrophies with various endocrinopathies such as gigantism, stunted growth, acromegaly and dystrophia adiposogenitalis. Thyroid disturbance,[1] parathyroid insufficiency,[9] changes in the pineal gland[11] and pluriglandular abnormalities[2] have also been noted, as have hypoglycemia and deficient glycogenesis.[5, 6] Ironside[5] stated that the inherited defect responsible for the development of muscular dystrophy may also be the cause of the endocrine disturbance of secondary and less important nature.

In a series of 36 cases of primary myopathy, Hurwitz[4] noted thyroid enlargement, a small sella turcica, undescended testes and adiposogenital dystrophy, but felt that the changes were too infrequent to assume an endocrine disturbance as the cause of muscular dystrophy. He showed, however, that altered carbohydrate metabolism occurs in the majority of patients with dystrophy. Similarly Wilson, [13] while noting the frequency of hypoglycemia and deficient glycogenesis, attributed the presence of endocrine disturbances to coincidence.

Several studies on retinitis pigmentosa suggest pituitary dysfunction may play an etiologic role.[6, 7, 10, 12] Moehlig and Pino[8] found high-arched palate in 100 per cent of 21 patients with retinitis pigmentosa, 14 per cent of whom were offspring of consanguinous parents. They related high arching of the hard palate to disturbances in its common embryologic development with the pituitary. They also pointed out the close embryologic and anatomical associations between the pituitary, hypothalamus and retina and felt that pituitary function is involved in retinitis pigmentosa.

In Givner's and Bruger's series[3] of 14 patients with retinitis pigmentosa, 11 had creatinuria (eight were males). There was a high incidence of nerve deafness and of high-arched palate. They reviewed the literature and concluded that the disease is hereditary and due to autonomic and endocrine dysfunction. Wortis and Shaskan[14] found consanguinity in 6 per cent and deafness in 44 per cent of 41 patients with retinitis pigmentosa. There were associated changes such as persistent amenorrhea, polydactylism, obesity and thyrotoxicosis. They felt that retinitis pigmentosa is only a sign of a more generalized disturbance.

Paget's disease, chronic occlusive arterial disease and various nervous and ocular disorders have been described in connection with pigmentary degeneration of the retina. A review of the literature has disclosed no case of progressive muscular dystrophy associated with retinitis pigmentosa. For this reason and because of the possible relation of each of the two disorders to endocrine disturbance, a description of a patient with both diseases was thought to be of interest.

CASE REPORT

A 68-year-old unmarried white male entered the Los Angeles County General Hospital on June 9, 1948. From very early childhood he had been unable to see at night except for distinguishing light from dark. Vision was apparently normal during the day. Sight progressively became poorer, terminating in blindness in 1940.

From the Los Angeles County General Hospital.